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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,852	11/12/2003	Gary L. Griffiths	IMMU:019US1	6078

37013 7590 03/11/2010

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
03/11/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ptomail@rkmlegalgroup.com

Office Action Summary	Application No.	Applicant(s)	
	10/706,852	GRIFFITHS ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/21/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9-18,20,21,23-35,38-40,42-55,57-89 and 91-125* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9,10,20,21,28,30,32,33,35,38,39,42,44,52,55,62,66-69,86,87 and 119-125* is/are rejected.

7)☒ Claim(s) *11-18,23-27,29,31,34,40,43,45-51,53,54,57-61,63-65,70-85,88,89 and 91-118* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 20, 2009 has been entered.

Claim 41 has been canceled. Claims 1, 9-18, 21, 23-35, 38-40, 42-55, 57-89 and 91-125 are pending. Claims 42-55, 57-89 and 91-124, previously withdrawn from consideration are hereby rejoined for examination. Claims 1, 9-18, 20, 21, 23-35, 38-40, 42-55, 57-89 and 91-125 are pending and under consideration.

It is noted that the effective priority date for the instant claims is commensurate with the disclosure of provisional application, 60/478,830, filed June 17, 2003. As stated in a previous Action

The '816 application makes only one reference to an anti-CD74 antibody found in claim 33. There is no further reference in the specification, and no written description of a genus of antibodies which bind to the LL1 epitope, no description of a PEG-lipid formulated into a liposome and conjugated to a anti-CD74 antibody, no description of a composition comprising the genus of antibodies of claim 11 with the exception of anti-CD22. Further, 10/314,330 makes no mention of the LL1 antibody, and therefore does not provide an adequate written description of the instant genus of antibodies now claimed which bind to the same epitope of CD74 that is bound by the LL1 antibody. Application 09/590,284 fails to provide an adequate written description of the genus of one or more antibodies further comprised by the instant claim 11. The 10/377,122 application describes the LL1 antibody and the antibodies of claim 11, but fails to describe the PEG-lipid liposome which is conjugated to the CD74 antibody. Accordingly, the effective priority date for the instant application is commensurate with the disclosure of provisional application, 60/478,830, filed June 17, 2003.

It is further noted that the 09/590,284 application, now U.S. 7,074,403, discloses bi-specific antibodies comprising CD22 and CD74 antibodies, and diabodies thereof, does not teach triabodies or tetrabodies comprising CD74 antibodies.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 54, 86, 87 and 119-124 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "one or more of the additional antibodies" in claim 54 lacks antecedent basis in claim 43. For purpose of examination, claim 54 will be read as dependent upon claim 53.

The recitation of "the" additional composition" in claim 86 lacks antecedent basis in claim 42.

It is unclear how the contacting of a carrier with a chimeric, human or humanized anti-CD74 antibody in claim 119 pertains to the objective of a method of preparing a carrier because said carrier is prepared by the mixing of one or more amphiphilic lipids with an effector. the further contacting of the formed carrier with the antibody is superfluous to the objective of preparing the carrier because it said carrier is already formed before contact with the antibodies.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9-13, 20, 21, 25, 26, 29-30, 32, 33, 35, 38, 39, 42, 44, 51-55, 57, 59, 60, 62, 63, 66, 67, 71-74, 84-89, 91, 93, 94, 96-98, 100-102, 106-108, 118, 119, 121 and 123-125 are rejected under 35 U.S.C. 103(a) as being obvious over Goldenberg et al (U.S. 7,074,403) as evidenced by Hoaruau et al (U.S. 2004/0076683) in view of Lundberg et al (Int Journal of Pharmaceutics, 1996, Vol. 134, pp. 119-127, reference 56 of the IDS fled November 20, 2004)

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claim 1 is drawn in part to a composition comprising one or more anti-CD74 antibodies or antigen-binding fragments thereof which bind to the LL1 epitope of CD74, wherein the anti-CD74 antibodies or antigen binding fragments thereof are covalently bound to the PEG component of a PEG-lipid conjugate incorporated into a liposome; wherein one or more effectors

are incorporated into a liposome in unmodified active form; wherein said anti-CD74 antibodies are humanized and wherein the anti-CD74 antibody or antigen-binding fragment thereof is an anti-CD74 diabody. Claim 9 embodies the composition of claim 1 wherein the one or more anti-CD74 antibodies or antigen binding fragments thereof are conjugated to the liposome by one or more of a sulfide linkage and an ester linkage. Claim 10 embodies the composition of claim 1 wherein the anti-CD74 antibodies are conjugated to the liposome by a sulfide linkage. Claim 11 embodies the composition of claim 1 further comprising a CD22 antibody. Claim 12 embodies the composition of claim 11 wherein the additional antibodies or fragments thereof are covalently bound to the PEG component of the PEG-lipid conjugate incorporated into a liposome. Claim 13 embodies the composition of claim 1 wherein the lipid component of the PEG-lipid conjugate is amphiphilic. Claim 20 embodies the composition of claim 1 wherein the effector comprises a therapeutic agent. Claim 21 embodies the composition of claim 1 wherein the effector comprises an immunoeffector or a cytokine. Claim 22 embodies the composition of claim 1 wherein the effector comprises a drug, enzyme, immunomodulator or a cytokine. Claim 25 embodies the composition of claim 1 comprising Group III, Group IV, Group V, transition, lanthanide or actinide metal cations. Claim 26 embodies the composition of claim 1 comprising Re, Cu, Au or At cations, or mixtures thereof. Claim 28 embodies the composition of claim 1 wherein the effector comprises a radionuclide. Claim 29 embodies the composition of claim 28 wherein the radionuclide is 32P, 67Cu, 90Y, 125I, 131I, 186Re, 188Re, 198Au or 211At of mixtures thereof. Claim 30 embodies the composition of claim 1 wherein the effector comprises an enzyme. Claim 32 embodies the composition of claim 1 wherein the effector comprises an immunomodulator. Claim 33 embodies the composition of claim 32 wherein the immunomodulator is selected from a group including Il-2 and GM-CSF. Claim 35 embodies the composition of claim 1 wherein the antigen-binding fragment thereof is conjugated to one or more therapeutic agents, diagnostic agents or mixtures thereof. Claim 38 embodies the composition of claim 1 wherein the anti-CD74 antibody or antigen-binding fragment thereof comprises a fusion protein comprising scFv. Claim 39 embodies the composition of claim 38 wherein the fusion protein is multivalent. Claim 125 is drawn to a kit comprising the composition of claim 1.

Claim 42 is drawn to a method for treating a disease or disorder comprising administering to a patient a therapeutic composition comprising one or more anti-CD74 antibodies or antigen-binding fragments thereof which bind to the LL1 epitope of CD74, wherein the anti-CD74 antibodies or antigen binding fragments thereof are covalently bound to the PEG component of a PEG-lipid conjugate incorporated into a liposome; wherein one or more effectors are incorporated into a liposome in unmodified active form; wherein said anti-CD74 antibodies are humanized and wherein the anti-CD74 antibody or antigen-binding fragment thereof is an anti-CD74 diabody. Claim 44 embodies the method of claim 42 wherein the disease or disorder is selected from the group consisting of an immune dysregulation disease, an autoimmune disease, an organ graft rejection, and graft versus host disease. Claim 51 embodies the method of claim 42 wherein the composition is administered i.v. or i.m. at a dose of 20-5000 mg. Claim 52 embodies the method of claim 42 wherein the composition comprises LL1 or a fragment thereof. Claim 53 embodies the method of claim 42 wherein the composition further comprises an anti-CD22 antibody or fragment thereof. Claim 54 specifies that the ati-CD22 antibody is conjugated to one or more of the lipids, polymeric carriers, micelle, nanoparticles or combinations thereof. Claim 55 embodies the method of claim 42 wherein the effector molecule comprises one or more drugs, prodrugs, toxins, enzymes, radioisotopes, immunomodulators, cytokines, hormones, antibodies , oligonucleotides or combinations thereof.. Claim 59 embodies the method of claim 42 wherein the composition further comprises cation selected from Group II, Group III, Group IV, Group V, transition, lanthanide or actinide metal cations. Claim 60 embodies the method of claim42 wherein the composition further comprises cation including Re, Cu, Au and At. Claim 62 embodies the method of claim 42 wherein the composition comprises a radionuclide. Claim 63 embodies thee method of claim 62 wherein the radionuclide is 32P, 90Y, 125I, 131I, 186Re, 188Re, 198Au or 211At. Claim 64 embodies the method of claim 62 wherein the composition comprises an enzyme. Claim 66 embodies the method of claim 62 wherein the composition comprises an immunomodulator. Claim67 embodies the method of claim 66 wherein the immunomodulator comprises Il-2 and GM-CSF.. Claim 71 embodies the method of claim 42 wherein the composition comprises one or more diagnostic agents. Claim 72 embodies the method of claim 42 comprising a diagnostic radionuclide. Claim 73 embodies the method of claim 72 wherein the diagnostic radionuclide includes 67Cu, 125I or 131I. Claim 74 embodies

the method of claim 73 wherein the diagnostic radionuclide emits 25-4000keV gamma particles and/or positrons. Claim 84 embodies the method of claim 42 further comprising performing an operative procedure.

Claim 119 is drawn to a method of preparing a carrier comprising: missing one or more amphiphilic lipids with an effector to form a carrier; and contacting the carrier with a chimeric, human or humanized anti-CD74 antibody, wherein the anti-CD74 antibody or antigen-binding fragment thereof is an anti-CD74 diabody, triabody or tetrabody. Claim 121 embodies the method of claim 119 further comprising reducing the antibody. Claim 123 embodies the method of claim 119 wherein the effector comprising one or more drugs, prodrugs, toxins, enzymes, radioisotopes, immunomodulator, cytokines, hormone, antibodies, oligonucleotides or mixtures thereof. Claim 124 embodies the method of claim 119 further comprising mixing the carrier with one or more therapeutic or diagnostic agents.

Goldenberg et al teach a method of treating an individual suffering from Class III autoimmune diseases (column 10, lines 32-57) comprising the administration of a composition comprising the administration of a anti-CD22 antibody and a anti-CD74 antibody (column 1, line 63 to column 2, line 3) which meets the limitations of claim 11 and 53.. Goldenberg et al teach that a exemplary anti-CD74 antibody is the LL1 antibody (column 6, lines 8-9). Goldenberg et al teach functional bi-specific antibodies single chained antibodies called diabodies (column 7, line 39 and column 8, lines 3-5). Goldenberg et al teach the coupling of antibodies to a lipid emulsion (column 8, line 29) formed by reducing the antibody (column 9, line 15-17) and reacting the free thiol groups of the reduced antibody with a vinyl sulfone group at the distal PEG terminus (column 9, lines 4-8) which meets the specific limitation of claim 121. Goldenberg et al teach humanized or human antibodies of the invention (column 6, lines 33-52). Goldenberg et al teach the antibodies of the invention carrying a radioisotope such as 195Au, 32P, 125I, 131I, 90Y, 186Re, 188Re, 67Cu and 211At which meets the limitations of claims 25, 26, 28, 29, 59, 60, 62 and 63. Goldenberg et al teach that the preferred radionuclides are beta, alpha and auger emitters in the range of 80 keV-500 keV (column 4, lines 9-11) which meets the limitations of claims 74 and 108. Goldenberg et al teach that the lipid emulsion comprises an oil core of triglyceride (column 8, lines 33-34) which meets the specific embodiment of claim 13 requiring a lipid component which is amphiphilic, as evidenced by Hoarau et al (US

20040076683, paragraph [0024]). Goldenberg et al teach methods of treatment comprising the administration of the antibodies of the invention with a supplemental therapeutic composition which can be administered before, concurrently or after administration of the antibodies of the invention (column 10, lines 59-77). Goldenberg et al teach that drugs known to act on B cells and/or T cells are particularly useful in the multimodal treatment of Class III autoimmune disease, and that these drugs include fludarabine, doxorubicin, methotreaxate, DNAse I and RNAses (column 11, lines 35-58) which meets the specific requirements of drugs, toxins and enzymes in claims 21 and 55. Goldenberg et al teach that Il-2 and GM-CSF are also therapeutic which can be used in the multimodal treatment of the invention (column 12, lines 4) in combination which the antibodies of the invention as a separate component. Goldenberg et al teach that antibodies to CD22, CD20, CD19 and CD74 can be used as conjugates for the delivery of a therapeutic agent, in combination with the administration of the naked antibodies of the invention (column 11, lines 16-24). Goldenberg et al teach that the antibodies of the invention can be admistered by indigenous or intramuscular injection (column 12, lines 14-24), and that the dose of the administered antibody is 20mg to 2g, thus fulfilling the embodiments of claim 51. Goldenberg et al do not specifically teach that the effectors are incorporated into the lipids in unmodified active form.

Lundberg et al teach that submicron lipid emulsions containing amphipathic polyethylene glycol modified phosphatidylethanolamine exhibit prolonged circulation time in vivo (abstract).

It would have been prima fake obvious at the time that the claimed invention was made to provide the effector agents taught by Goldenberg in the same lipid emulsion that was derivatized for attachment of the CD22-CD74 antibodies. One of skill in the art would have been motivated to do so by the teachings of Lundberg on the improvement in circulation time afforded by incorporation of active agents into lipid emulsions comprising polyethylene glycol ethanolamine. One of skill in the art would understand that the polyethylene glycol ethanolamine was the same lipid emulsion as utilized by Goldenberg et al for the delivery of the B cell antibodies comprising anti-CD22 with anti-CD74.

Claim 84 embodies the method of claim 42 further comprising performing an operative procedure. Goldenberg et al teach that spleenectomy was performed as part of the treatment of two patients (Examples 2 and 6) who received only the anti-CD22 antibodies. It would have

been prima facie obvious to combine spleenectomy with the lipid emulsions comprising anti-CD22 and anti-CD74 and therapeutic agents. One of skill in the art would have been motivated to do so because spleenectomy is a recognized treatment for some class III autoimmune disorders.

Claims 85-89, 91, 93, 94, 96-98, 100-102, 106-108 and 118 require the administration of additional compositions comprising the therapeutic agents taught by Goldenberg et al to be part of the invention. It would have been prima facie obvious at the time that the claimed invention was made to provide the therapeutic agents taught by Goldenberg et al to be useful for the treatment of class II autoimmune diseases in additional doses. One of skill in the art would have been motivated to do so because it is reasonable to assume that the first administration of a composition would not provide the optimal disease stabilization or reversal. One of skill in the art would understand that it is beneficial to provide therapeutic compositions over an interval of time in order to optimize the positive effect on the targeted diseases.

All other rejection and objections as set forth or maintained in the prior Office action are withdrawn in light of applicant's amendments.

Claims 14-18, 23, 24, 27, 31, 34, 40, 43, 45-50, 57, 58, 61, 65, 68-70, 75-83, 91, 92, 95, 99, 103-105, 109-117, 120 and 122 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Hong et al (Journal of Pharmacy and Pharmacology, January 2002, Vol. 54, pp. 51-58).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643